

The Structure of Some Condensation Products of Pulegone

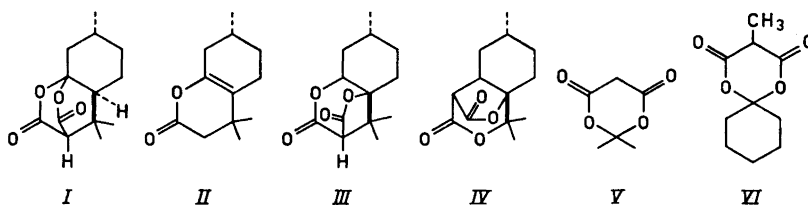
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Evidence is presented confirming the structures originally assigned by Vorländer *et al.*¹ to pulegone malonic acid ketodilactone and pulegone acetic acid anhydride. Pulegone acetone has been related to pulegone acetic acid anhydride and shown to have structure XV.

Vorländer *et al.*¹ condensed pulegone with sodiomalonic ester and obtained a compound that was hydrolysed to an acid which spontaneously lactonised to give "pulegone malonic acid ketodilactone", formulated as I^a. On repeated distillation, carbon dioxide was evolved giving "pulegone acetic acid anhydride" formulated as the enol lactone II^b. "Pulegone malonic acid ketodilactone" and "pulegone acetic acid anhydride" have been prepared by Vorländer's procedure and subjected to further investigations.

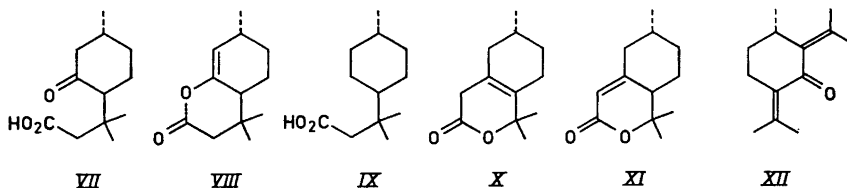
The dilactone I, containing only six-membered lactone groups, exhibited an unusual infrared absorption with bands at 1775 and 1805 cm^{-1} (in CCl_4). Therefore structures containing five-membered lactone groups such as III or IV could not be excluded. The dilactone was stable to chromic acid oxidation² and did not consume periodate in neutral solution. The ketodilactone appears to exist as a dicarboxylate in neutral solution. The calcium salt of the dicarboxylic acid corresponding to I shows absorption bands at 1700 cm^{-1} (keto group) and 1330, 1570 cm^{-1} (carboxylate), and regenerates I upon acidification.



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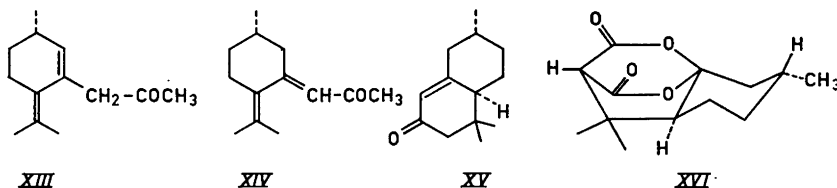
The abnormally high carbonyl absorptions of the ketodilactone are worthy of comment. Many instances have been discussed where the carbonyl absorption of esters and lactones show a higher frequency than expected³. 1,1-D. acetoxypropane absorbs at a higher frequency (1761 cm^{-1})⁴ than ethyl acetate (1733 cm^{-1})⁶ while cyclic esters of the general type (V) show two carbonyl bands, for example, isopropylidenemalonate (V) absorbs at 1750 and 1787 cm^{-1} (in chloroform)⁷ while cyclohexylidene methylmalonate (VI) shows bands at 1755 and 1790 cm^{-1} .^{5,8} The ketodilactone I embraces the structural features of several of these substances and this fact might explain the observed abnormality.

Controlled pyrolysis of I at $250\text{--}290^\circ$ followed by distillation under reduced pressure, rather than repeated distillation^{1b} afforded the crystalline pulegone acetic acid anhydride (II) in high yield. The compound II exhibited an I.R. absorption typical of enol lactones⁹ and gave pulegone acetic acid (VII) on alkaline hydrolysis^{1b}. The alternative structure (VIII) is ruled out by the fact that the N.M.R. spectrum (at 40 Mc/s , benzene as internal standard) showed no sign of a hydrogen attached to an ethylenic bond. The proton signals observed were: (i) a sharp band at 167.5 c.p.s. (2 protons) due to the methylene group adjacent to the carbonyl group, (ii) a band at 219 c.p.s. (9 protons) due to the three methyl substituents and (iii) two diffused bands centered at 182 c.p.s. (7 protons). The enol lactone II was very resistant to catalytic hydrogenation and was only slowly hydrogenated to give *p*-menthyl-8-acetic acid (IX). The isomeric lactones X and XI have recently been synthesised¹⁰ and differ distinctly from Vorländer's enol lactone.



Pulegone condenses with ethyl acetoacetate under varying conditions^{11,12} to give a compound, pulegene acetone, for which several structures have been suggested (XII—XIV). Repetition of the condensation under acidic conditions (zinc chloride-glacial acetic acid)¹¹ gave two crystalline compounds. One was shown to be the material obtained previously (m.p. $74\text{--}76^\circ$)^{11,1} and the other, a new condensation product, will be described in a future report. The I.R. and U.V. absorption of pulegene acetone are incompatible with any of these formulations but seemed to fit structure XV. The formation of this compound would be easily understandable, assuming 1,4-addition of ethyl acetoacetate to pulegone followed by acetolysis, decarboxylation and ring closure. That structure XV is correct was shown by relating it to II in the following manner. The enol lactone II reacted with methyl magnesium iodide to give a product which was treated with alkali¹³ to effect ring closure. The oily reaction product was transformed to pulegene acetone (XV) in excellent yield by zinc chloride treatment. The absolute configuration of pulegone is

known¹⁴ and this ketone on reduction with sodium and alcohol¹⁵ yields D-(—)-menthone in which the side chains are trans. It is therefore probable that the ketodilactone I possesses the absolute configuration XVI.



After completion of this work Wolinski and Tyrell¹⁶ also presented evidence confirming the structure XV for pulegene acetone. Their chemical approach is essentially the reverse of that in this report.

EXPERIMENTAL

U.V. spectra and specific rotations are taken in 95 % ethanol. M.p.'s were taken on a Kofler block. Light petroleum refers to a fraction of boiling range 40–60°.

Pulegone malonic acid ketodilactone (I). The compound was prepared according to Vorländer and Köthner^{1a} from pulegone (Fluka, $[\alpha]_D + 22^\circ$). M.p. 103–105°, $[\alpha]_D + 12^\circ$. $\nu_{\text{max}}^{\text{CCl}_4}$ 1775 and 1805 cm^{-1} , $\nu_{\text{max}}^{\text{KBr}}$ 1760 and 1795 cm^{-1} , λ_{max} 208–212 $\text{m}\mu$ (ϵ 400).

The calcium salt of pulegone malonic acid was prepared by adding calcium acetate solution to an alkaline solution of the dilactone. The precipitate was collected, washed with ether, 15 % ammonium chloride solution and then with water and dried over P_2O_5 . ν_{max} 1570 and 1700 cm^{-1} . On acidification the salt gave the dilactone (I).

Oxidation experiments. (1) A mixture of the dilactone (1.5 g), CrO_2 (3.5 g), acetic acid (30 ml) and conc. sulphuric acid (1 ml) was kept at 50° for 24 h and then diluted with water and the pH adjusted to ca. 4. The precipitate (1 g) was unchanged starting material. (2) The dilactone (1 g) was dissolved in 2 N sodium hydroxide solution and pH adjusted to 6–7. Sodium periodate (4.5 g) in water (25 ml) was added. After 20 h at room temperature the solution was acidified. Unchanged dilactone (880 mg) was recovered.

Pulegone acetic acid anhydride (II). The ketodilactone I (4.2 g) was pyrolysed at 240–290° for 30 min and the residue was distilled under a reduced pressure giving the main fraction, b.p. 110–115°/12 mm, (3.5 g) which was recrystallised from light petroleum. The compound, m.p. 46–47°, (lit.^{1b} 46°, $[\alpha]_D + 71.6^\circ$ (EtOH)), $[\alpha]_D + 72.2^\circ$, $\nu_{\text{max}}^{\text{CCl}_4}$ 1420, 1695 and 1770 cm^{-1} , ν_{max} 214 $\text{m}\mu$ (ϵ 3400).

Pulegone acetic acid (VII). The sublimed compound had m.p. 70–72° [$\alpha]_D - 3^\circ$ (lit.^{1b} 67–68°), $[\alpha]_D - 3.2^\circ$. $\nu_{\text{max}}^{\text{CCl}_4}$ 1705, 2700 and 3400 cm^{-1} in CCl_4 . Semicarbazone, crystals from ethanol, m.p. 188–190°, ν_{max} 230 $\text{m}\mu$ (ϵ 12 400).

p-Menthyl-8-acetic acid (IX). Pulegone acetic acid anhydride (900 mg) in acetic acid (25 ml) was hydrogenated (PtO_2) for 16 h. The uptake of hydrogen was very slow. Addition of water gave an oil which was dissolved in ether. Shaking the ether extract with potassium carbonate solution extracted an acid which was recrystallised from methanol: water (5:1), m.p. 90–92°, $[\alpha]_D \pm 0$. (Found: C 72.47; H 11.40. Calc. for $\text{C}_{12}\text{H}_{22}\text{O}_2$: 72.68; H 11.18). ν_{max} 1695, 2700–3200 cm^{-1} .

Pulegene acetone (XV). Pulegone acetic acid anhydride (4 g) in benzene (50 ml) was added, at room temperature, to the Grignard reagent from methyl iodide (4 g) and magnesium (650 mg) in ether (35 ml). The mixture was heated for one hour under reflux. 2 N HCl (30 ml) was added and the aqueous phase was shaken with ether. The combined organic phases were successively shaken with water. Methanol (50 ml) and 50 % NaOH solution (7 ml) were added to the residue from the evaporation of the ether-benzene solution. After 2 h at room temperature, most of the methanol was evaporated *in vacuo*

and water (50 ml) added. The product obtained was distilled *in vacuo* giving two fractions (a) and (b). (b.p. 107–112°/10 mm, 3.12 g, and b.p. 115–130°/10 mm, ca. 0.25 g, respectively). Fraction (b) crystallised on cooling and was recrystallised from light petroleum to give white crystals identified as pulegone acetone. Fraction a has the following properties: $\nu_{\max}^{\text{liquid}}$ 1675 and 1625 cm^{-1} , λ_{\max} 241 $\text{m}\mu$ (ϵ 5100) and 324 (ca. 100).

A solution of fraction a (1.7 g) and fused zinc chloride (3 g) in acetic acid (20 ml) was heated on a steam bath for 7 h. Extraction with light petroleum gave a residue which was distilled under reduced pressure, b.p. 130–132°/8 mm (1.4 g). The oil crystallised upon cooling. The product was recrystallised three times from light petroleum, m.p. 74–76°, undepressed on admixture with pulegone acetone prepared according to Barbier¹¹ $[\alpha]_{\text{D}}$ –126°, ν_{\max}^{KBr} 885, 1424, 1622 and 1665 cm^{-1} , $\nu_{\max}^{\text{CCl}_4}$ 1635 and 1675 cm^{-1} , λ_{\max} 240.5 $\text{m}\mu$ (ϵ 15 100). (Found: C 81.28; H 10.31. Calc. for $\text{C}_{13}\text{H}_{20}\text{O}$: C 81.20; H 10.48). Semicarbazone, crystals from ethanol, m.p. 177–179°, λ_{\max} 269 $\text{m}\mu$ (ϵ 22 000). 2,4-Dinitrophenylhydrazone crystals from ethanol m.p. 140–141°, ν_{\max} 381 $\text{m}\mu$ (ϵ 24 800).

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REFERENCES

1. (a) Vorländer, D. and Köthner, E. *Ann.* **345** (1906) 154.
(b) Vorländer, D., May, A. and König, W. *Ibid.* 188.
2. Corey, E. J., Ohno, M., Chow, S. W. and Scherrer, R. A. *J. Am. Chem. Soc.* **81** (1959) 6305.
3. Bellamy, L. J. *The Infrared Spectra of Complex Molecules*, 2nd ed., Chapt, 11, Methuen, London 1958.
4. Rasmussen, R. S. and Brattain, D. R. *J. Am. Chem. Soc.* **71** (1949) 2073.
5. Jones, R. N. and Herling, F. *J. Org. Chem.* **19** (1954) 1252.
6. Felton, D. G. I. and Orr, S. F. D. *J. Chem. Soc.* **1955** 2170.
7. Snyder, H. R. and Krause, C. W. *J. Am. Chem. Soc.* **80** (1958) 1942.
8. Personal communication from Professor B. Eistert to whom the author is much indebted.
9. Rosenkranz, H. and Gut, M. *Helv. Chim. Acta* **36** (1953) 1000.
10. Mousseron, M., Mousseron-Canet, M. and Meyrolles, J. *Compt. rend.* **251** (1960) 2447.
11. Barbier, P. *Compt. rend.* **127** (1898) 870.
12. Jupp, L. G., Kon, G. A. R. and Lockton, E. H. *J. Chem. Soc.* **1928** 1639.
13. Heard, R. D. H. and Ziegler, P. *J. Am. Chem. Soc.* **73** (1951) 4636.
14. Fredga, A. *Tetrahedron* **8** (1960) 126.
15. Simonsen, J. L. and Owen, L. N. *The Terpenes*, Vol. I, p. 373, Cambridge University Press 1947.
16. Wolinski, P. and Tyrrell, Ann M. *Chem. & Ind. London* **1960** 1104.

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